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48/00, A61P 31/14, A61K 38/53, 38/21W2 1NY (GB). **KNAPP, Susanne** [GB/GB]; Imperial
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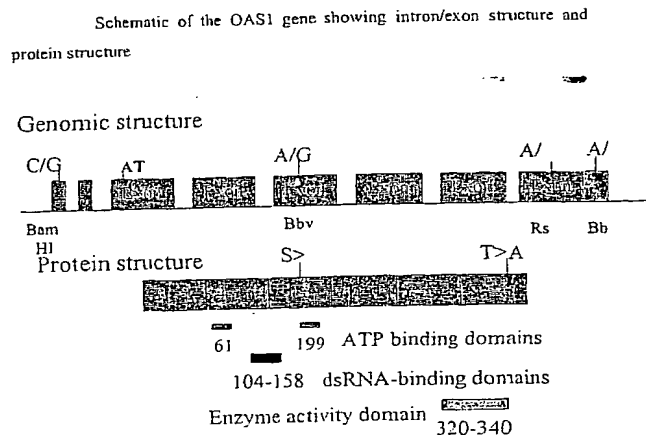
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[Continued on next page]

(54) Title: METHODS OF TREATMENT AND DIAGNOSIS OF PATIENTS WITH HEPATITIS C INFECTION



(57) Abstract: Use of a compound capable of modulating the level of activity of the OAS gene and/or activity of the OAS protein, in the manufacture of a medicament for the treatment of a patient with or at risk of hepatitis C infection, wherein the compound is not an interferon or an isoprenoid, such as geranylgeranylacetone (GGA). A method of screening for compounds for treating HCV infection, wherein a cell is treated with a test compound and any change in OAS gene activity and/or OAS protein activity or level is assessed, wherein the compound is not an interferon or an isoprenoid, such as geranylgeranylacetone (GGA). Use of a compound capable of modulating the level of activity of the RNase L gene and/or activity of the RNase L protein, in the manufacture of a medicament for the treatment of a patient with or at risk of hepatitis C infection, wherein the compound is not an interferon or an isoprenoid, such as geranylgeranylacetone (GGA). A method of screening for compounds for treating HCV infection, wherein a cell is treated with a test compound and any change in RNase L gene activity and/or RNase L protein activity or level is assessed, wherein the compound is not an interferon or an isoprenoid, such as geranylgeranylacetone (GGA).

WO 03/089003 A1



— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Inte onal Appl No
PCT/GB 03/01625

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K45/00 G01N33/50 A61K31/7088 C12Q1/68 A61K38/53
A61K48/00 A61P31/14 //(A61K38/53, 38:21)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	V. CARREÑO ET AL.: "Randomized controlled trial of recombinant human granulocyte-macrophage colony-stimulating factor for the treatment of chronic hepatitis C." CYTOKINE, vol. 12, no. 2, February 2000 (2000-02), pages 165-170, XP002250567	1-5, 36
Y	page 168, left-hand column, last paragraph page 169, left-hand column, paragraph 1 --- -/--	1-5, 8-12, 22-24, 31-36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

8 August 2003

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INTERNATIONAL SEARCH REPORT

Int. Application No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, Y	WO 02 090552 A (HALLE JOERN-PETER ; REGENBOGEN JOHANNES (DE); SWITCH BIOTECH AG (DE) 14 November 2002 (2002-11-14) page 4, line 16 -page 6, line 10; claims page 36, line 11 -page 47, line 3 ---	1-5, 8-12, 22-24, 31-36
A	L. RUSCH ET AL.: "Monitoring activation of ribonuclease L by 2',5'-oligoadenylates using purified recombinant enzyme and intact malignant glioma cells." METHODS IN ENZYMOLOGY, vol. 342, 2001, pages 10-20, XP008020481 cited in the application the whole document ---	1-5, 8-12, 15-19, 22-36
A	S. N. SARKAR ET AL.: "Production, purification, and characterization of recombinant 2',5'-oligoadenylate synthetases." METHODS, vol. 15, XP002250569 cited in the application the whole document ---	1-5, 8-12, 15-19, 22-36
A	T. ICHIKAWA ET AL.: "Geranylgeranylacetone induces antiviral gene expression in human hepatoma cells." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 280, 2001, pages 933-939, XP002250570 ORLANDO, FL, US cited in the application page 938, right-hand column, last paragraph ---	1-5, 8-12, 15-19, 22-36
A	WO 02 06343 A (PEPGEN CORP) 24 January 2002 (2002-01-24) page 10, line 1 - line 14; claims; examples -----	1-5, 8-12, 15-19, 22-36

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/GB 03/01625

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 35 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Continuation of Box I.2

Claims Nos.: 1(p),6,7,8(p),13,14,15(p),20,21,22-25(p),32-36(p). "p" = partly

Present claims (all partly) 1,8,15,22-25 and 32-36 relate to the use of, and compositions comprising, compounds defined by reference to a desirable characteristic or property, namely their capability of modulating the level of activity of the OAS, RNase L or 2'-5' phosphodiesterase gene and/or protein, and to the use of, and compositions comprising, nucleic acids having the capability to selectively hybridize to an OAS nucleic acid.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search for the above mentioned claims has been carried out based on the general inventive concept as disclosed in the description of the application.

"Claims 6,7,13,14,20,21 and partly claims 32-35 (as far as being dependent on claims 6,14 or 21) encompass a genus of compounds defined only by their function wherein the relationship between the structural features of the members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the as-filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could have assayed a compound of interest using the claimed assays does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound (other than those that might be particularly disclosed in an application) would fall within the scope of what is claimed. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity. Therefore, no search has been performed for claims 6,7,13,14,20,21 and partly claims 32-35 (as far as being dependent on claims 6,14 or 21). (Art. 5 and Art. 6 PCT)".

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/01625

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02090552	A	14-11-2002	DE 10122206 A1 WO 02090552 A2	28-11-2002 14-11-2002
WO 0206343	A	24-01-2002	AU 7705501 A WO 0206343 A2 US 2003049277 A1	30-01-2002 24-01-2002 13-03-2003